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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,362	12/28/2006	Yukihide Iwamoto	4456-0106PUS1	3478

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EXAMINER

POPA, ILEANA

ART UNIT	PAPER NUMBER
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1633

NOTIFICATION DATE	DELIVERY MODE
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02/22/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/566,362	Applicant(s) IWAMOTO ET AL.	
	Examiner ILEANA POPA	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 December 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

- 1, Claim 3 has been amended. Claims 7-12 are new.
Claims 1-12 are pending and under examination.
2. The rejection of claim 3 for lacking antecedent basis in claim 1 is withdrawn in response to Applicant's amendments to the claim filed on 12/03/2009.

Response to Arguments

Information Disclosure Statement

3. Applicant indicates that the provided document WO 01/48148 is the published PCT application corresponding to JP-2003-518379. However, "corresponding" does not mean that WO 01/48148 is the English translation of the JP-2003-518379 document. In the absence of an English translation, the Examiner is unable to determine whether the disclosures of the WO 01/48148 document is identical to the disclosure of the JP-2003-518379.

Priority

4. Acknowledgment is made of Applicant's submission of an English language translation of the foreign priority document 2003-283703 filed in JAPAN on 1/28/1005.

Claim Rejections - 35 USC § 102

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5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1 and 4-6 remain rejected under 35 U.S.C. 102(b) as being anticipated by Britt et al. (Arch. Otolaryngol. Head Neck Surg., 1998, 124: 671-677).

Britt et al. teach an *ex vivo* method of preparing an autologous tissue-engineered cartilage by seeding autologous chondrocytes onto the surface of a polymeric scaffold by placing the polymers into a mold and allowing them to dry (i.e., the scaffold is shaped into a desired form), seeding and adhering the cells onto the scaffold, and culturing the cell-scaffold composite in a medium comprising 10% fetal calf serum (i.e., in the presence of growth factors) to induce the formation of neocartilage (i.e., under conditions which induce differentiation of cells into a cartilage tissue) (claims 1, 5 and 6) (Abstract; p. 671, column 2; p. 672, column 2; p. 673, column 1). Britt et al. teach their scaffold as having micropores (claim 4) (p. 672, column 1, last paragraph). Since Britt et al. teach all claim limitations, the claimed invention is anticipated by the above-cited art.

7. Claims 2-6 remain rejected under 35 U.S.C. 102(b) as being anticipated by van Susante et al. (Biomaterials, 2001, 22: 2359-2369).

van Susante et al. teach a method of preparing an artificial joint by seeding and adhering chondrocytes onto the surface of a porous collagen matrix shaped into a

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desired form, culturing the chondrocyte-matrix composite in a medium comprising 10% fetal calf serum (i.e., in the presence of growth factors), wherein the chondrocytes secrete extracellular matrix components and form a cartilage tissue (claims 2, 3, 5 and 6) (Abstract; p. 2361, columns 1 and 2; paragraph bridging p. 2363 and p. 2364, Fig. 2, and column 2, p. 2366, columns 1 and 2). van Susante et al. also teach that their collagen matrix has micropores (claim 4) (p. 2360, column 2). Since van Susante et al. teach all claim limitations, the claimed invention is anticipated by the above-cited art.

Applicant traversed the instant rejections on the grounds that neither Britt nor van Susante teaches or suggests "adhering cell masses onto the surface of a carrier" shaped into a desired form and culturing the cell masses, as in the claimed invention. The "cell masses" recited in independent claims 1 and 2 are cell aggregation masses or spheroids formed by cells adhering to each other. See page 5, lines 2-4 of the specification.

Britt and van Susante only disclose cells (not cell masses) adhered to the surface of a carrier, which cells are further cultured. Britt at page 673, under the heading "CHONDROCYTE SEEDING OF POLYMER TEMPLATES," discloses that a volume of isolated chondrocyte solution was applied to the polymer template in an effort to achieve a cell concentration of $1 \text{ to } 2 \times 10^7/\text{cm}^3$ of template material, van Susante at page 2361, under the heading "2.3. Chondrocyte isolation and seeding," discloses that sponges were seeded with $100 \mu\text{l}$ of a cell suspension containing 850,000 chondrocytes, followed by gentle centrifugation of the entire plate (3 min, 600g), which

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revealed optimal penetration of the cells into the pores at the air-side of the sponges. All of these disclosures by Britt and van Susante teach that cells (not cell masses) are adhered to the surface of a carrier and cultured.

Thus, Britt and van Susante do not disclose each and every element of the claimed invention, and Applicant requests that the rejections of claims 1-6 as being anticipated by the cited art be withdrawn.

Applicant's arguments are acknowledged; however, the rejection is maintained for the following reasons:

Applicant argues that both Britt and van Susante teach seeding cell suspension and not cell masses, as required by the claims. This is not found persuasive because the claims do not require seeding cell masses. The only requirement in the claims is adhering cell masses to a support. How cell masses are obtained is irrelevant, as long as the cell masses adhere to the support. As the instant specification and the art teach that, when cells in suspension are seeded on solid supports, they adhere to each other to form cell masses (see the instant specification, p. 4, line 33 to p. 5, line 4; Anderer et al., Journal of Bone and Mineral Research, 2002, 17: 1420-1429, Applicant's IDS, p. 1421, column 1, second full paragraph). Therefore, the cells of Britt and van Susante form cell masses after being seeded on the support, which cell masses adhere to the support. For these reasons, it is concluded that Britt and van Susante teach all claim limitations and the rejections are maintained.

New Rejections

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderer et al. (Journal of Bone and Mineral Research, 2002, 17: 1420-1429, Applicant's IDS), in view of each Tsutsumi et al. (Exp. Biol. Med., 2002, 227: 402-411, Abstract), Long et al. (WO 01/48148, Applicant's IDS), Hoffmann et al. (J. Cell Sci., 2001, 115: 769-781) and van Susante.

Anderer et al. teach a method of producing a cartilage, the method comprising adhering chondrocytes masses onto human femoral condyles (i.e., a curved carrier shaped into a desired form or into a desired joint) and culturing the chondrocytes masses in medium comprising fetal calf serum (i.e., in the presence of TGF- β , see Tsutsumi et al., Abstract) to induce fusion of the cell masses and the formation of neocartilage (i.e., under conditions which induce differentiation of the chondrocytes masses into a cartilage tissue); the cell (claims 1-3, 5, 6 and 10-12) (Abstract, p. 1421, paragraph bridging columns 1 and 2, p. 1424, columns 1 and 2).

Anderer et al. do not teach a carrier comprising calcium triphosphate, wherein the carrier comprises pores with a diameter of 10-500 μ (claims 4, 7 and 8). Long et al. teach producing a cartilage by growing cell masses such as C3/H101/2 cell masses

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(i.e., murine mesenchymal stem cells, see Hoffmann et al., Abstract) on carriers made of calcium triphosphate (p. 3, p. 4, fourth paragraph, p. 10, second full paragraph, p. 13, second paragraph, p. 28, last paragraph, p. 29). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Anderer et al. by replacing their carrier with the calcium triphosphate carrier of Long et al. and/or replacing their chondrocytes masses with mesenchymal stem cell masses to achieve the predictable result of obtaining a cartilage.

Anderer et al. and Long et al. teach murine mesenchymal stem cells and not teach mesenchymal stem cells derived from human bone marrow (claim 9). However, it would have been obvious to one of skill in the art, at the time the invention was made, to replace their mesenchymal stem cells with mesenchymal stem cells derived from human bone marrow to achieve the predictable result of obtaining a cartilage suitable for implantation in humans.

Anderer et al. and Long et al. do not specifically teach their carrier as being porous. However, doing such is suggested by the prior art. For example, van Susante et al. teach obtaining cartilage by growing chondrocytes on carriers having pores with a diameter of 50-100 μ (p. 2360, paragraph bridging columns 1 and 2, p. 2363, column 1, first paragraph). Based on these teachings, one of skill in the art would have known that carriers having pores with a diameter of 50-100 μ are suitable to be used in the method of Anderer et al. and Long et al. and would have found it obvious to adhere their chondrocytes masses to such carriers to achieve the predictable result of obtaining a cartilage.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Primary Examiner, Art Unit 1633